REMARKS

Prior to entry of the foregoing amendment, claims 1-21 and 35 are pending in this application. Claims 7 and 21 are canceled by the present amendment. Independent claims 1 and 35 recite "an intimate admixture of azithromycin and a stabilizing-effective amount of an antioxidant." Upon entry of the present amendment, claims 1-6, 8-20 and 35 remain pending.

A. Rejections Under § 102

Claims 1-6, 13 and 35 stand rejected under 35 U.S.C. § 102(a) as being anticipated by U.S. Patent Nos. 6,239,112 (Macy et al.) and 6,239,113 (Dawson et al.). Applicants traverse these rejections.

Macy describes a water-miscible pharmaceutical composition containing up to about 40% of a macrolide such azithromycin in a non-aqueous water miscible organic solvent system. The composition, as disclosed at col. 7, lines 30-34, may contain an antioxidant. Example 2 describes a composition containing sodium metabisulfite as an antioxidant. The dry ingredients in Example 2 are combined and the liquid components are added while stirring until a clear solution is obtained. The non-aqueous water miscible organic solvent system is a 40/60% v/v mixture of glycerol formula/propylene glycol.

Dawson describes an ophthalmic composition of an azalide antibiotic for topical application to the eye. At col. 6, lines 7-14, *Dawson* discloses that the ophthalmic composition may contain "antioxidants." Among the disclosed forms of the ophthalmic composition are included "depots" that provide sustained release of the azalide antibiotic to the eye. Depots are disclosed in more detail beginning at col. 7, lines 15+.

The presently rejected claims are directed to a "stabilized azithromycin composition comprising an intimate admixture of azithromycin and a stabilizing effective amount of an antioxidant." As explained in the specification of the subject application, azithromycin is subject to degradation during manufacture and storage, including manufacture and storage of pharmaceutical dosage forms, especially at elevated temperatures.

Neither *Macy* nor *Dawson* discloses an "intimate admixture" of azithromycin and a stabilizing effective amount of an antioxidant. At best, *Macy* and *Dawson* disclose a simple mixture of azithromycin and an antioxidant. The simple admixture that is disclosed in both *Macy* and *Dawson* is neither taught nor suggested to result in a "stabilized azithromycin composition," i.e., a composition wherein no more than about 3.8% w/w of the azithromycin degrades at 55°C for 7 days or (2) no more than 1.25% degrades at 50 °C for 20 hours. Indeed, the subject specification, at page 30, lines 30-36 states that simple powder mixing, of the type disclosed in *Macy* and *Dawson* does not result in the additional stability provided when the azithromycin and antioxidant are formed as an "intimate admixture," e.g., by co-precipitation or co-milling, in accordance with the present invention.

Because neither Macy nor Dawson discloses each and every element of claims 1-6, 13 and 35, it is respectfully submitted that the rejection of these claims under 35 U.S.C. § 102(a) should be withdrawn, which action is respectfully requested.

B. Rejections Under § 103

Claims 1-6, 8-20 and 35 stand rejected under 35 U.S.C. § 103 as being obvious over *Macy* or *Dawson* in view of U.S. Patent No. 5,605,889 (Curatolo et al.). Applicants respectfully traverse this rejection.

Claims 7 and 21, which are now canceled, were rejected under 35 U.S.C. § 103 as being obvious over *Macy* or *Dawson* in view of U.S. Patent No. 6,365,574 (Singer et al.). Cancellation of claims 7 and 21 by the present invention renders this rejection moot.

As discussed above, neither *Macy* nor *Dawson* discloses an "intimate admixture" of azithromycin and a stabilizing effective amount of an antioxidant. At best, *Macy* and *Dawson* disclose a simple mixture of azithromycin and an antioxidant. However, the simple admixture that is disclosed in both *Macy* and *Dawson* is neither taught nor suggested to result in a "stabilized azithromycin composition," i.e., a composition wherein no more than about 3.8% w/w of the azithromycin degrades at 55°C for 7 days or (2) no more than 1.25% degrades at 50 °C for 20 hours. Indeed, the subject specification, at page 30, lines 30-36 states that simple

powder mixing, of the type disclosed in *Macy* and *Dawson*, does not result in the additional stability provided when the azithromycin and antioxidant are formed as an "intimate admixture," e.g., by co-precipitation or co-milling, in accordance with the present invention. as that .

There is no disclosure in either *Macy* or *Dawson* evidencing a recognition of the need to protect the azithromycin component of the compositions disclosed therein against degradation by including an antioxidant, let alone an antioxidant in "intimate admixture" with the azithromycin component. It is respectfully submitted that the general teaching of including an antioxidant in the compositions of *Macy* and *Dawson*, therefore, cannot render obvious the presently claimed invention directed to a particular "intimate admixture" of the antioxidant and the azithromycin that results in a "stabilized azithromycin composition," wherein the azithromycin component has enhanced stability against degradation relative to a simple powder mixture of azithromycin used to make pharmaceutical compositions and/or dosage forms. Simply stated, a person having ordinary skill in the art would not be motivated in view of either *Macy* or *Dawson* to form an intimate admixture of azithromycin with a reasonable expectation of forming a "stabilized azithromycin composition" as that term is used in the context of the present invention.

Curatolo does not address the deficiencies of either *Macy* or *Dawson*. Curatolo is relied on simply for its teaching of making a tablet dosage form of azithromycin. There is no disclosure in Curatolo evidencing a recognition of the need to protect the azithromycin component of the compositions disclosed therein against degradation by including an antioxidant, let alone an antioxidant in "intimate admixture" with the azithromycin component.

In view of the foregoing, Applicants submit that a *prima facie* case of obviousness has not been established and respectfully request withdrawal of the rejection.

C. Double Patenting

Claims 1-21 and 35 were rejected on the ground of obviousness-type double patenting over claims 1-21 and 35 of U.S. Patent No. 6,764,997. This rejection is moot as to claims 7 and 21, which have been canceled by the present amendment.

Applicants submit herewith a terminal disclaimer obviating this ground of rejection.

CONCLUSION

Applicants respectfully submit that the present application is now in condition for allowance, which action is earnestly solicited. The Examiner is invited to contact Applicants' representative to discuss any issue that would expedite allowance of this application.

The Commissioner is authorized to charge all required fees, fees under § 1.17, or all required extension of time fees, or to credit any overpayment to Kenyon & Kenyon's Deposit Account No. 11-0600.

Respectfully submitted,

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February 22, 2006

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